

AMENDMENTS TO THE CLAIMS

1. (Original) A method for increasing plasminogen activation, said method comprising contacting a solution containing pro-urokinase plasminogen activator (pro-uPA) with melanotransferrin (p97) or an enzymatically active fragment thereof for a time sufficient to cause increased plasminogen activation.
2. (Original) The method of claim 1, wherein said p97 increase plasminogen activation and fibrinolysis through tissue plasminogen activator (t-PA).
3. (Original) A method for inhibiting plasminogen activation, said method comprising the step of contacting pro-urokinase plasminogen activator (pro-uPA) with membrane bound melanotransferrin (p97) for a time sufficient to prevent plasminogen activation.
4. (Original) A method for preventing cell migration, said method comprising the step of contacting a cell expressing melanotransferrin (p97) on its surface with exogenous soluble 97 or an antibody, or an antigen binding fragment thereof, directed to said p97 expressed on the surface of said cell, said soluble p97 competing with the p97 expressed on the cell surface, activating plasminogen in solution instead of membrane-bound plasminogen, thus preventing cell migration, said antibody, or active fragment thereof binding p97 on the surface of the cell thus preventing activation of membrane-bound plasminogen, preventing cell migration.
5. (Original) The method of claim 4, wherein the antibody is a monoclonal antibody.

6. (Original) The method of claim 5, wherein said monoclonal antibody is selected from the group consisting of L235, HybC, HybE, HybF, 9B6 and 2C7.
7. (Original) The method of claim 5, wherein said monoclonal antibody is L235.
8. (Original) The method of claim 4, wherein said cell is a tumor cell.
9. (Original) The method of claim 4, wherein said cell is selected from the group consisting of human vascular or microvascular endothelial cells and human melanoma cells.
10. (Original) A method for treating cancer caused by cells expressing melanotransferrin (p97) at their surface, said method comprising the step of administering to a patient in need thereof exogenous soluble p97 or an antibody an antibody, or active fragment thereof, directed to said p97 expressed on the surface of said cell, said soluble p97 competing with the p97 expressed on the cell surface, activating plasminogen in solution instead of membrane-bound plasminogen, thus preventing cell migration, said antibody, or active fragment thereof binding p97 on the surface of the cell thus preventing activation of membrane-bound plasminogen, preventing cell migration, preventing cancer cells from spreading.
11. (Original) The method of claim 10, wherein the antibody is a monoclonal antibody.

12. (Original) The method of claim 11, wherein said monoclonal antibody is selected from the group consisting of L235, HybC, HybE, HybF, 9B6 and 2C7.

13. (Original) The method of claim 11, wherein said monoclonal antibody is L235.

14. (Original) The method of claim 10, wherein said cell is a tumor cell.

15. (Original) The method of claim 10, wherein said cell is selected from the group consisting of human vascular or microvascular endothelial cells and human melanoma cells.

16. (Original) A method for regulating capillary tube formation, said method comprising the step administering to a patient in need thereof soluble 97, wherein said soluble p97 prevents or reduces capillary tube formation and thus angiogenesis.

17. (Original) The method according to claim 16, wherein said administering is carried out orally, parenterally, subcutaneously, intravenously, intramuscularly, intraperitoneally, intraarterially, transdermally or via a mucus membrane.

18. (Original) A pharmaceutical composition for use in regulating activation of plasminogen, said composition comprising a therapeutically effective amount of melanotransferrin (p97) or an enzymatically active fragment thereof in association with a pharmaceutically acceptable carrier.

19. (Original) The pharmaceutical composition of claim 18, wherein said p97 is soluble p97 for increasing activation of plasminogen.

20. (Original) A method of regulating the activation of plasminogen, comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 18.

21. (Original) The method according to claim 20, wherein said administering is carried out orally, parenterally, subcutaneously, intravenously, intramuscularly, intraperitoneally, intraarterially, transdermally or via a mucus membrane.

22. (Original) A pharmaceutical composition for use in regulating cell migration of a cell showing p97 activity, comprising a therapeutically effective amount of one of p97, an enzymatically active fragment thereof, or an antibody recognizing specifically p97, or an antigen binding fragment thereof, in association with a pharmaceutically acceptable carrier.

23. (Original) The pharmaceutical composition of claim 22, wherein said p97 is exogenous soluble p97 for preventing cell migration.

24. (Original) The pharmaceutical composition of claim 22, wherein the antibody is a monoclonal antibody.

25. (Original) The pharmaceutical composition of claim 24, wherein said monoclonal antibody is selected from the group consisting of L235, HybC, HybE, HybF, 9B6 and 2C7.

26. (Original) The pharmaceutical composition of claim 24, wherein said monoclonal antibody is L235.

27. (Original) A method of regulating cell migration of a cell showing p97 activity, comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 22.

28. (Original) The method of claim 27, wherein the cell showing p97 activity is a tumor cell.

29. (Original) The method of claim 27, wherein said cell is selected from the group consisting of human vascular or microvascular endothelial cells and human melanoma cells.

30. (Original) The method of claim 27, wherein said p97 is exogenous soluble p97 for preventing cell migration.

31. (Original) The method of claim 27, wherein said administering is carried out orally, parenterally, subcutaneously, intravenously, intramuscularly, intraperitoneally, intraarterially, transdermally or via a mucus membrane.

32. (Original) A pharmaceutical composition for use in treating cancer comprising a therapeutically effective amount of one of melanotransferrin (p97), an enzymatically active fragment thereof, or an antibody recognizing specifically p97, or an antigen binding fragment thereof, in association with a pharmaceutically acceptable carrier.

33. (Original) The pharmaceutical composition of claim 32, wherein the antibody is a monoclonal antibody.

34. (Original) The pharmaceutical composition of claim 33, wherein said monoclonal antibody is selected from the group consisting of L235, HybC, HybE, HybF, 9B6 and 2C7.

35. (Original) The pharmaceutical composition of claim 33, wherein said monoclonal antibody is L235.

36. (Original) A method of treating cancer, comprising administering to an individual a therapeutically effective amount of a pharmaceutical composition according to claim 32.

37. (Original) The method according to claim 36, wherein said administering is carried out orally, parenterally, subcutaneously, intravenously, intramuscularly, intraperitoneally, intraarterially, transdermally or via a mucus membrane.

38. (Original) The method according to claim 36, wherein said cancer is selected from the group consisting of melanoma, prostate cancer, leukemia, hormone dependent cancer, breast cancer, colon cancer, lung cancer, skin cancer, ovarian cancer, pancreatic cancer, bone cancer, liver cancer, biliary cancer, urinary organ cancer (for example, bladder, testis), lymphoma, retinoblastoma, sarcoma, epidermal cancer, liver cancer, esophageal cancer, stomach cancer, cancer of the brain, cancer of the kidney, and metastasis thereof.

39. (Original) A pharmaceutical composition for use in regulating angiogenesis comprising a therapeutically effective amount of melanotransferrin (p97) or an enzymatically active fragment thereof in association with a pharmaceutically acceptable carrier.

40. (Original) A method of regulating angiogenesis, comprising administering to an individual a pharmaceutically effective amount of a pharmaceutical composition according to claim 39.

41. (Original) The method according to claim 40, wherein said administering is carried out orally, parenterally, subcutaneously, intravenously, intramuscularly, intraperitoneally, intraarterially, transdermally or via a mucus membrane.

Claims 42-51. (CANCELLED).

52. (Original) A method for treating thrombo-embolic disorders, said method comprising the step of administering to a patient in need thereof exogenous soluble p97, said soluble p97 increasing clot permeability and dissolution, thereby treating said thrombo-embolic disorders.

53. (Original) The method of claim 52, wherein said disorders are selected from the group consisting of venous or arterial thrombosis, thrombophlebitis, pulmonary or cerebral embolism, thrombotic microangiopathy and intravascular clotting.

54. (Original) The method of claim 53, wherein said disorders cause heart or cerebral strokes.